LISTING OF THE CLAIMS

1. (Currently Amended) A method of assessing a patient's risk of having a fetus with a fetal abnormality comprising:

determining the patient's *a priori* risk of having a fetus with the fetal abnormality;

determining a bi-parietal diameter to occipito-frontal diameter (BPD/OFD) ratio of a patient's fetus during a first trimester of pregnancy;

determining an at least one secondary marker measurement corresponding to the patient~~, wherein the BPD/OFD ratio and the at least one secondary marker measurement are determined at a same trimester of pregnancy~~ during a first trimester of pregnancy;

performing a comparison of the BPD/OFD ratio of the patient's fetus and the at least one secondary marker measurement corresponding to the patient with observed relative frequency distributions of fetal BPD/OFD ratios and at least one secondary marker measurements from observed affected and observed unaffected pregnancies; and

assessing the patient's risk of having a fetus with a fetal abnormality in view of a result of the comparison and the patient's *a priori* risk of having a fetus with the fetal abnormality, wherein the fetal abnormality is a craniofacial abnormality, a chromosomal abnormality, or a developmental central nervous system abnormality.

2. (Original) The method of claim 1, wherein the fetal abnormality is a chromosomal abnormality.

3. (Original) The method of claim 2, wherein the chromosomal abnormality is a trisomic abnormality.

4. (Previously Presented ) The method of claim 3, wherein the trisomic abnormality is Down Syndrome, trisomy 13, or trisomy 18.

5. (Previously Presented ) The method of claim 1, wherein the fetal abnormality

developmental central nervous system abnormality is open spinal bifida.

6. (Currently Amended) A method of assessing a patient's risk of having a fetus with a fetal abnormality comprising:

determining the patient's *a priori* risk of having a fetus with the fetal abnormality;

determining a bi-parietal diameter to occipito-frontal diameter (BPD/OFD) ratio of a patient's fetus comprising measuring or obtaining measurements of an occipito-frontal diameter and a bi-parietal diameter of the patient's fetus during a first trimester of pregnancy;

determining an at least one secondary marker measurement corresponding to the patient during a first trimester of pregnancy;

performing a comparison of the BPD/OFD ratio of the patient's fetus and the at least one secondary marker measurement corresponding to the patient with observed relative frequency distributions of fetal BPD/OFD ratios and at least one secondary marker measurements from observed affected and observed unaffected pregnancies; and

assessing the patient's risk of having a fetus with a fetal abnormality in view of a result of the comparison and the patient's *a priori* risk of having a fetus with the fetal abnormality, wherein the fetal abnormality is a chromosomal abnormality, a craniofacial abnormality, or a developmental central nervous system abnormality.

7. (Original) The method of claim 1, wherein determining the at least one secondary marker measurement corresponding to the patient comprises measuring or obtaining measurements of a biochemical marker from the fetus or the patient.

8. (Original) The method of claim 7, wherein the biochemical marker is selected from a group consisting of total human chorionic gonadotropin, alpha fetoprotein, unconjugated estriol, total estriol, pregnancy associated placental protein A, inhibin A, free beta hCG, free alpha hCG, and hyperglycosylated hCG.

9. (Original) The method of claim 1, wherein determining the at least one secondary

marker measurement corresponding to the patient comprises measuring or obtaining measurements of an ultrasound marker from the fetus.

10. (Original) The method of claim 9, wherein the ultrasound marker is selected from a group consisting of nuchal translucency, nuchal fold thickness, femur length, humerus length, hyperechogenic bowel, renal pyelectasis, fetal heart rate, echogenic foci, ductus venosus blood flow, absent or hypoplastic nasal bone, intra-uterine growth retardation, exomphalos, and micrognathia.

11. (Original) The method of claim 1, wherein the at least one secondary marker measurement corresponding to the patient and the at least one secondary marker measurements from the observed affected and the observed unaffected pregnancies are each a plurality of secondary marker measurements.

12. (Original) The method of claim 1, wherein performing the comparison comprises: grouping the fetal BPD/OFD ratios from the observed affected and the observed unaffected pregnancies into pre-determined categories of BPD/OFD ratios; deriving likelihood ratios for each of the pre-determined categories; and assigning the patient one of the likelihood ratios based on the one of the pre-determined categories that corresponds to the BPD/OFD ratio of the patient's fetus.

13. (Original) The method of claim 1, wherein performing the comparison comprises: grouping the at least one secondary marker measurements from the observed affected and the observed unaffected pregnancies into pre-determined categories of secondary marker measurements; deriving likelihood ratios for each of the pre-determined categories; and assigning the patient one of the likelihood ratios based on the one of the predetermined categories that corresponds to the at least one secondary marker measurement corresponding to the patient.

14. (Previously Presented) The method of claim 1, wherein performing the comparison comprises:

grouping the fetal BPD/OFD ratios from the observed affected and the observed unaffected pregnancies into pre-determined category of fetal BPD/OFD ratios;

deriving a first set of likelihood ratios for each of the pre-determined category of fetal BPD/OFD ratios;

assigning to the patient a first likelihood ratio from the first set of likelihood ratios based on the one of the pre-determined categories of fetal BPD/FD ratios that corresponds to the BPD/OFD ratio of the patient's fetus;

grouping the at least one secondary marker measurements from the observed affected and the observed unaffected pregnancies into pre-determined categories of secondary marker measurements;

deriving a second set of likelihood ratios for each of the pre-determined categories of secondary marker measurements;

assigning to the patient a second likelihood ratio from the second set of likelihood ratios based on the one of the pre-determined categories of secondary marker measurements that corresponds to the at least one secondary marker measurement corresponding to the patient; and

multiplying the patient's first likelihood ratio by the second likelihood ratio to obtain an overall likelihood ratio.

15. (Original) The method of claim 1, wherein performing the comparison comprises deriving a likelihood ratio for the patient using a multivariate statistical analysis.

16. (Original) The method of claim 15, wherein the multivariate statistical analysis comprises a multivariate Gaussian analysis.

17. (Original) The method of claim 1, further comprising normalizing the at least one secondary marker measurement corresponding to the patient and the at least one secondary marker measurements from the observed affected and the observed unaffected

pregnancies for gestational age prior to performing the comparison.

18. (Original) The method of claim 17, wherein normalizing comprises expressing the at least one secondary marker measurement corresponding to the patient and the at least one secondary marker measurements from the observed affected and the observed unaffected pregnancies as a multiple of the median measurement in unaffected pregnancies of the same gestational age.

19. (Original) The method of claim 1, wherein determining the BPD/OFD ratio of the patient's fetus comprises calculating a delta value thereof and performing the comparison comprises comparing the delta value of the BPD/OFD ratio of the patient's fetus to delta values of fetal BPD/OFD ratios from the observed affected and the observed unaffected pregnancies.

20. (Original) The method of claim 1, wherein determining the at least one secondary marker measurement corresponding to the patient comprises calculating a delta value thereof and performing the comparison comprises comparing the delta value of the patient's at least one secondary marker measurement to delta values of the at least one secondary marker measurements from the observed affected and the observed unaffected pregnancies.

21. (Original) The method of claim 1, wherein performing the comparison comprises: determining a first delta value of the BPD/OFD ratio of the patient's fetus; deriving a first set of likelihood ratios for pre-determined categories of delta values of BPD/OFD ratios; assigning to the patient a first likelihood ratio from the first set of likelihood ratios based on the one of the pre-determined categories of delta values of BPD/OFD ratios that corresponds to the patient's first delta value; determining a second delta value of the at least one secondary marker measurement corresponding to the patient; deriving a second set of likelihood ratios for pre-determined categories of delta values of secondary marker measurements; assigning to the patient a second likelihood ratio from the second set of

likelihood ratios based on the one of the pre-determined categories of delta values of secondary marker measurements that corresponds to the patient's second delta value; multiplying the first likelihood ratio by the second likelihood ratio to obtain an overall likelihood ratio.

22. (Original) The method of claim 1, wherein performing the comparison comprises comparing a mathematical transformation of the BPD/OFD ratio of the patient's fetus to a mathematical transformation of the fetal BPD/OFD ratios from the observed affected and the observed unaffected pregnancies.

23. (Original) The method of claim 22, wherein the mathematical transformation of the BPD/OFD ratio of the patient's fetus and the mathematical transformation of the fetal BPD/OFD ratios from the observed affected and the observed unaffected pregnancies each comprises a logarithm.

24. (Original) The method of claim 22, wherein the mathematical transformation of the BPD/OFD ratio of the patient's fetus and the mathematical transformation of the fetal BPD/OFD ratios from the observed affected and the observed unaffected pregnancies each comprises a square root.

25. (Original)The method of claim 1, wherein performing the comparison comprises comparing a mathematical transformation of the at least one secondary marker measurement corresponding to the patient to a mathematical transformation of the at least one secondary marker measurements from the observed affected and the observed unaffected pregnancies.

26. (Original) The method of claim 25, wherein the mathematical transformation of the at least one secondary marker corresponding to the patient and the at least one secondary marker from the observed affected and the observed unaffected pregnancies each comprises a logarithm.

27. (Original)The method of claim 25, wherein the mathematical transformation of the at least one secondary marker corresponding to the patient and the at least one secondary marker from the observed affected and the observed unaffected pregnancies each comprises a square root.

28. (Currently Amended) A method of assessing whether a patient is screen-positive or screen-negative for having a fetus with a fetal abnormality, the method comprising:

selecting a risk cut-off level for determining whether a patient is screen-positive or screen-negative for having a fetus with a fetal abnormality;

determining a BPD/OFD ratio of the patient's fetus and at least one secondary marker measurement corresponding to the patient;

calculating a likelihood ratio of the patient based on the BPD/OFD ratio of the patient's fetus and the at least one secondary marker measurement corresponding to the patient; multiplying the patient's likelihood ratio by the patient's *a priori* risk to determine the patient's risk of a fetal abnormality; and

assessing whether the patient is screen-positive or screen-negative by comparing the patient's risk of a fetal abnormality to the risk-cut off level, wherein if the patient's risk is greater than or equal to the risk-cut off level, then the patient is screen-positive and if the patient's risk is less than the risk cut-off level, then the patient is screen-negative.

29. (Currently Amended) A method of assessing a patient's risk of having a fetus with a fetal abnormality, the method comprising: determining an OFD/BPD ratio of a patient's fetus; determining at least one secondary marker measurement corresponding to the patient;

performing a comparison of the OFD/BPD ratio of the patient's fetus and the at least one secondary marker measurement corresponding to the patient with observed relative frequency distributions of fetal OFD/BPD ratios and at least one secondary marker measurements from observed affected and observed unaffected pregnancies; and

assessing the patient's risk of having a fetus with a fetal abnormality in view of a

result of the comparison and the patient's *a priori* risk of having a fetus with the fetal abnormality.

30. (Currently Amended) A machine-readable medium having stored thereon a plurality of executable instructions, the plurality of executable instructions comprising:

receiving or calculating a BPD/OFD ratio of a patient's fetus during a first trimester of pregnancy;

receiving at least one secondary marker measurement corresponding to the patient during a first trimester of pregnancy;

performing a comparison of the BPD/OFD ratio of the patient's fetus and the at least one secondary marker measurement corresponding to the patient with observed relative frequency distributions of fetal BPD/OFD ratios and at least one secondary marker measurements from observed affected and observed unaffected pregnancies;

assessing the patient's risk of having a fetus with a fetal abnormality in view of a result of the comparison and the patient's *a priori* risk of having a fetus with the fetal abnormality.

31. (Previously Presented) The method of claim 4, wherein the trisomic disorder is Down's Syndrome.

32. (Previously Presented) The method of claim 1, wherein the chromosomal abnormality is triploidy.

33. (Previously Presented) The method of claim 6, wherein the fetal abnormality is a chromosomal abnormality.

34. (Previously Presented) The method of claim 33, wherein the chromosomal abnormality is triploidy.

35. (Previously Presented) The method of claim 33, wherein the chromosomal

abnormality is a trisomic abnormality.

36. (Previously Presented) The method of claim 35, wherein the trisomic abnormality is Down Syndrome, trisomy 13, or trisomy 18.

37. (Previously Presented) The method of claim 36, wherein the trisomic abnormality is Down Syndrome.

38. (Previously Presented) The method of claim 6, wherein the developmental central nervous system abnormality is open spinal bifida.